Protein Interaction Networks in Health & Disease

In the past decade, numerous comprehensive proteomics studies have allowed researchers to generate detailed protein-protein interaction ("interactome") maps, providing an unparalleled global view of the interplay between the different systems within the cell, and greatly increasing our understanding of the physiological mechanisms involved in both normal and disease states.

My lab is focused specifically on understanding how the interactions of membrane proteins contribute to cellular disease states at a systems level. Despite extensive proteomics research in the past decade, there is a lack of in-depth understanding of protein networks associated with integral membrane proteins because of their unique biochemical features, enormous complexity and multiplicity. This is a major obstacle to understanding the biology of deregulation of integral membrane proteins which leads to numerous human diseases, and consequently hinders our development of improved and more targeted therapies to help treat these diseases.

To address this problem, my lab has developed two unique technologies specifically suited for the study of full-length integral membrane proteins in their natural cellular context; the classic Membrane Yeast Two-Hybrid (MYTH) [1-5] and the newly created Mammalian Membrane Two-Hybrid (MaMTH)[6]. Our ultimate goal is to uncover a wealth of information about protein interactions for the majority of "druggable" human membrane proteins, which should in turn greatly facilitate the discovery of new truths about diseases like cancer, schizophrenia, cystic fibrosis, hypertension and Parkinson's disease.

During my talk, I will discuss our recent findings indicating that the application of MaMTH to the human Epidermal Growth Factor Receptor (EGFR) resulted in the identification of Crk II protein as a novel interactor of oncogenic EGFR (L858R), and showed that CRKII promotes persistent activation of aberrant signaling in non-small cell lung cancer (NSCLC) cells. I will also illustrate how MaMTH is a powerful tool for investigating dynamic interactomes of human integral membrane proteins and why it promises significant contributions to therapeutic research.

Selected references

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